

REMARKS

Claims 1-23, 26-27 and 29 were pending. Claims 4, 7-8, 10-11, 16-23, 26, 27 and 29 have been cancelled without prejudice to pursuing these claims in this or other continuing applications. Claims 30-31 are newly added. Claims 1-3, 5, 9, and 12-15 have been amended. Upon entry of the present amendments, Claims 1-3, 5, 9, 12-15 and 30-31 will be pending in this application and under active consideration.

The claims have been amended to more particularly and distinctly claim that which Applicants regard as their invention. In particular, Claim 1 is amended to recite steps (a) and (b) as requested by the Examiner. Claims 2-3, 5, 9, 12-15 have been amended to correct minor informalities therein.

Claims 30-31 are newly added. In particular, Claim 30 is added to recite that steps (a) and (b) can be performed simultaneously. Support for this claim can be found in the specification, *inter alia*, on page 13, lines 5-16. Claim 31 is added to recite that the milk is derived from a transgenic mammal. Support for this claim can be found in the specification, *inter alia*, on page 10, lines 5-6.

These amendments do not constitute new matter as defined in 35 U.S.C. § 132. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

I. Formal Matters

A. Restriction Requirement

The Examiner has issued a restriction requirement among the claims of this invention. Applicants have elected the species of Claims 1-15 for prosecution in this application. Accordingly, Claims 16-23, 26-27, and 29, which are directed to the non-elected species, are cancelled from this application. Applicants reserve rights to pursue these claims in this or other continuing applications.

B. Claim Objections

In the office action, page 2 (Paper No. 13), the Examiner objects to Claims 5 and 7 as being substantial duplicates. Applicants' amendment of Claim 5 and cancellation of Claim 7 render Examiner's objection to these claims moot.

II. Claim Rejections Under 35 U. S. C. § 112, Second Paragraph

In the office action, page 3 (Paper No. 13), the Examiner rejects Claims 1-15 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention.

In particular, the Examiner rejects Claims 1 and 3 as having no clear method steps. Also, the Examiner object to the language "transfer of protease enzyme into the whey phase" of Claim 6. Additionally, the Examiner objects the language of Claim 15 as being confusing.

Applicants have amended Claim 1 to recite the method steps, as required by the Examiner, and amended Claim 3 to be dependent on Claim 1. Additionally, Applicants have cancelled Claims 4, 6-8, 10-11, and amended Claims 1-3, 5, 9, 12-15 to delete the language objected to by the Examiner and to correct the antecedent basis of these claims. Accordingly, in view of the amendment to these claims, Applicants submit that the Examiner's rejections of these claims have been overcome.

Reconsideration and withdrawal of this rejection is respectfully requested

III. Claim Rejections Under 35 U. S. C. § 103

In the Office Action, page 4 (Paper No. 13) the Examiner rejects Claims 1-15 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Garner *et al.* (US 5,639,940) in view of Tripodi (WO 9213495) and further in view of Vukovich *et al.* (1980) and Lord (US 6,037,457).

In particular, the Examiner asserts that Garner *et al.* discloses the transgenic production of fibrinogen in milk of various livestock and collection and recovery of fibrinogen from the milk using precipitation, filtration and protein chromatography. While

the Examiner believes that Garner *et al.* does not teach the method of precipitating fibrinogen from milk in the presence of lysine, a lysine analog, ϵ -aminocaproic acid, or the specific HIC chromatography, it is the Examiner's position that Tripodi, Vukovich *et al.*, and Lord cure this deficiency.

Specifically, the Examiner alleges that Tripodi discloses precipitating fibrinogen from plasma with PEG in a buffer containing ϵ -aminocaproic acid. The Examiner further alleges that Vukovich *et al.* teaches that fibrinogen can be highly purified using HIC and Lord teaches that recombinantly produced fibrinogen can be purified by various techniques known in the art including precipitation and HIC.

The Examiner asserts that one of ordinary skill in the art at the time the invention was made would have been motivated to purify fibrinogen transgenically produced in milk according to Garner *et al.* by precipitation from the milk in the presence of one or more of lysine, lysine analog, or ϵ -aminocaproic acid as taught by Tripodi and further process fibrinogen through HIC chromatography as taught by Vukovich *et al.* and Lord. Applicants respectfully traverse the Examiner's rejections for the following reasons.

Applicants respectfully submit that the references cited by the Examiner, either alone or in combination, does not teach or suggest the two-step method of protein purification of the invention as claimed. Applicants respectfully submit that the two-step method of the present invention is surprisingly and unexpectedly effective in purifying milk proteins.

Garner *et al.* discloses the transgenic production of fibrinogen. Although this reference mentions that fibrinogen is collected and recovered from milk using standard practices such as precipitation, filtration and protein chromatography, as noted by the Examiner, no specific technique for any of these general methods for the recovery of fibrinogen from milk is disclosed. Nowhere in Garner *et al.* is the two-step method of purification of fibrinogen of the invention as claimed taught or suggested. Neither of the secondary references cited by the Examiner cures the deficiency of Garner *et al.* to arrive at the claimed invention.

Tripodi teaches precipitating fibrinogen from plasma using polyethylene glycol (PEG) in a buffer containing ϵ -aminocaproic acid. Although Tripodi uses ϵ -aminocaproic acid in precipitating fibrinogen from plasma, ϵ -aminocaproic acid is used as part of a buffer whose principal precipitant is PEG. The purification technique used in Tripodi involves precipitation with PEG followed by a second step of PEG precipitation and followed by the treatment of

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the precipitate with glycine. Applicants submit that the teaching of Tripodi defeats the purpose of the invention because the use of PEG causes precipitation of both casein and fibrinogen together and therefore makes it impossible to separate these milk proteins.

Applicants have unexpectedly found that ϵ -aminocaproic acid has superior properties in preventing degradation of milk fibrinogen. Fibrinogen is very unstable and can not be successfully precipitated in the presence of protease enzymes present in milk. *See*, the specification, *inter alia*, at page 4, lines 10-19. Also, as the biochemical composition of milk is radically different from plasma, it was highly unexpected that ϵ -aminocaproic acid would be useful in preventing degradation of fibrinogen during purification from milk. *See*, the specification, *inter alia*, at page 22, lines 1-12.

Vulkovich *et al.* teaches that fibrinogen may be highly purified using HIC. However, Vulkovich *et al.* does not teach or suggest the two-step method of protein purification of the invention as claimed.

Lord teaches that recombinantly produced fibrinogen can be purified from serum-free medium using various techniques known in the art, those listed include precipitation or HIC (see, column 6, lines 36 - 52). Lord does not teach or suggest the two-step method of protein purification of the invention as claimed.

For all the afore-mentioned reasons, Applicants respectfully submit that the combination of Garner *et al.* with any of the secondary references, even if properly made, which is not admitted, would not teach or suggest the two-step method of protein purification of the invention as claimed. Accordingly, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness against the claims of this invention.

Withdrawal and reconsideration of this rejection is respectfully requested.

CONCLUSION


In light of the above, Applicants respectfully submit that all pending claims are allowable over the art of record, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action mailed December 4, 2002 (Paper No. 13). The Examiner is invited and encouraged to contact the undersigned

Attorney Docket No.: 8117-14 (36941-150674)
Amendment and Reply Under 37 C.F.R. § 1.111

attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

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